Proteomics: The Promise of Proteomics for Personalized Medicine (Part 1 of 3)

Balintfy: This year, nearly one-point-five million Americans will receive the devastating news: they've been diagnosed with cancer. Also this year, more than half a million Americans will die of cancer. But today we know that early detection, diagnosis, and treatment are the best hope for long-term survival. Specifically, chances of surviving cancer are greater if it's diagnosed when still confined to the organ of origin—what's called stage 1. So researchers today are looking at proteomics, the study of proteins, as an early detection tool.

In part one of our three part series, we talk to Dr. Henry Rodriguez, the director of the Clinical Proteomic Technologies for Cancer programs at the NCI. We start with some background. What is it that proteins do?

Dr. Rodriguez: What happens is, is that every cell happens to have, which is what people are very familiar with, is the DNA, but ultimately that DNA needs to form some functional unit that's going to have the different capabilities to carry signals throughout the cell and throughout the body. Those workhorses are what people refer to as the proteins. So it can be the DNA itself as this beautiful blueprint, but ultimately that blueprint has to form a product, and the vast majority of those products downstream are going to be the protein.

Balintfy: What's the importance of studying proteomics?

Dr. Rodriguez: Proteomics is very important to early cancer detection, both diagnosis also helps the treatment of cancer, and that in turn relates to personalized medicine. Because the belief there is that cancerous cells ultimately will shed proteins and other molecules into their surrounding environment, and if these proteins are shown to have clinical utility—this is what we refer to as biomarkers—the result of this is that the real greatest promise for early detection in the treatment of cancer lies in our ability to find biomarkers and if feasible, in bodily fluids that are going to be very easily accessible, such as blood and urine, which is also one that people go after.

Balintfy: We've actually talked about biomarkers before on the podcast. But you mentioned clinical utility and how proteins are biomarkers. Can you explain that a little bit more?

Dr. Rodriguez: Sure. So if you look at it today, right now there happens to be two main dominant protein biomarkers that people are quite familiar with that you could test in blood. There's actually more than two, but the main ones that people are quite familiar with happens to be both prostate-specific antigen, or PSA, and the other one has to be cancer antigen 125, commonly referred to as CA-125. Now, these are ones that actually have been FDA approved tumor associated antigens.

Unfortunately, both tests may result in false negatives, which is failing to detect cancer in those who have it, which is poor sensitivity, or false positive, which is testing positive for the presence of cancer in people who are actually cancer free, which is poor specificity.

But today we do know that tumor-associated proteins do exist in blood, and those are two good examples. While not the best, it does exist.

So what you have now is that the National Cancer Institute is actually working on ways to try to improve the current methodologies that we have, and hopefully in our ability to detect better protein biomarkers that could lead to early detection of cancer.

Balintfy: So if we can see the proteins, and we can see how they're biomarkers, then it leads to better tests for cancer. Is that an oversimplification?

Dr. Rodriguez: No, in fact that's a perfect way of saying it. I mean, today, we absolutely do know that the earlier you're able to detect cancer, the far better your survival rate's going to be. So proteomics is one of those fields that people recognize. Here are two examples, and are there other ones in this vast amount, this huge ocean they call proteomics, which is all the potential proteins that a cell in the body happens to have.

Balintfy: There are a lot of proteins in the body. I heard that anywhere from a quarter of a million to a million distinct proteins—

Dr. Rodriguez: That's right, so the best guesstimates could be as low as a quarter of a million or a million, but now if you throw into the factors that at the DNA level you have all these variations that could occur, that's going to lead to modifying base-up [proteins downstream. More importantly, when a protein's produced, the same protein itself can undergo multiple modifications, but that's the beauty of the whole proteomics, is that as these different proteins are modified, they carry out their unique functions. So it's not this easy to say there's only "x" amount. There's a huge ocean that's out there. That's great because that means there's a big target area to go after, but at the same time, it lends to tremendous complexity for us to be able to mine that huge amount of diversity that exists.

Balintfy: How do you study proteins? How are you able to see and look at something so small? Is there technology out there that allows you to study the little proteins?

Dr. Rodriguez: Yeah, so in the field of proteomics, there's two predominant platforms or technologies that happens to exist. One of them has to be mass spectrometry, and this is sort of this evolving, powerful, analytical technology that's out there. It actually allows scientists now to detect and identify ever-smaller amounts of these proteins. The method's very precise, and it's absolutely sensitive, and it has the ability to distinguish proteins at different composition by single-hydrogen atoms.

Now, the other platform uses nature's own ways of capturing proteins, and those are the ones referred to as protein microarrays. In the common press, people might refer to them as protein chips or biochips.

Now, what makes these unique is that they're able to measure a multitude of different proteins, but the way they do it is by developing capturing reagents, actually fish out the protein from a complex mixture. There's different ways of doing it, but the most common way of developing this affinity capture reagent is a monoclonal antibody, which is natural to every cell that's out there, or to biology.

Balintfy: It's an antibody, so that's something—it's another sort of biometric thing or—what exactly is an antibody?

Dr. Rodriguez: The easy way of looking at it is when you develop a disease, or let's say you get influenza, the body has to defend itself, so it develops these proteins that will actually capture that. So antibodies are actually that component itself, and what they do there is, as opposed to mass spectrometry, which is just engineering base component behind it, it measures the mass. When it comes to protein chips, they're actually using nature's own antibodies to capture very specifically what it was intended to go after all along.

Balintfy: Great. I think we're doing a good job of covering the broad topic of proteomics. Are there other things in this sort of introductory episode that you think are important to cover? Are there programs NCI is launching that deserve mention at this early stage?

Dr. Rodriguez: Yeah, so one of the things that I alluded to is that while I truly believe that proteomics is this very promising field, and it's going to have a huge impact, especially in the area of early diagnosis, I also alluded to that there are good examples that you can now detect proteins that can be used for the early diagnosis of specific cancers, but yet, they're not the best ones on top there. You know, so what NCI now has done, I think they've taken a very proactive and very bold move by launching in 2006, late 2006, this bold initiative that they refer to as Clinical Proteomic Technologies for Cancer Initiative.

People now refer to it as the CPTC, and what we're doing here is, simply, we're working very hard to improve the discovery and development of protein biomarkers and the way we're doing that is by trying to optimize the current technologies that are out there. At the same time, developing new technologies and systems to significantly advance the field of cancer proteomics research, and of course, the way we're going to do this is by establishing standards, rigorous quality control measures where that's going to be applicable.

Balintfy: And I think that's what we're going to get to more in the next episode, is that right?

Dr. Rodriguez: Absolutely, we'll go into more in depth, and I'll tell you the more great promises that the field has to offer.

Balintfy: Great, thank you very much.

Dr. Rodriguez: OK

Balintfy: Thanks again to Dr. Henry Rodriguez at NCI. For more information about the NCI Clinical Proteomic Technologies for Cancer Initiative, visit the website proteomics.cancer.gov. And be sure to tune in, in two weeks.